REMARKS

Applicants submit herewith a revised oath and declaration.

Claims 1-28, 30-34, 47-50 and 57-60 are pending in this application.

Applicants have cancelled claims 29, 35-46 and 51-56 without prejudice, and reserve their right to prosecute the subject matter of the cancelled claims in any future application claiming benefit or priority herefrom under 35 U.S.C. § 120.

Applicants have amended claims 1 and 47 to recite methods for repairing a defect locus in a nonarticular cartilage and promoting chondrogenesis at a nonarticular defect, respectively, comprising the step of administering an osteogenic device comprising an osteogenic protein of SEQ ID NO: 6 in a carrier, thereby inducing the formation of functional cartilage tissue, with the proviso that the osteogenic protein of SEQ ID NO: 6 may not be GDF-5 or GDF-6. Support for this amendment is provided at specification page 14, line 16 to page 17, line 10 and in claims 1, 29 and 47 as originally filed.

Applicants have amended claims 3, 4, 7, 10, 11, 15, 16, 21, 22, 30 and 31 to improve their form.

Applicants have amended claim 27 to delete the recitation of GDF-5, GDF-6, BMP-13 and BMP-14.

Applicants have amended claim 50 to depend from claim 47, instead of cancelled claim 49.

Applicants have amended claim 57 to depend from claims 1, 26, 47 and 50. Support for this amendment is provided in the claims as filed, and at specification page 20, lines 19-37.

None of the amendments adds new matter.

Applicants address the Examiner's rejection below:

Oath and Declaration

The Examiner states that the Oath and Declaration is defective because non-initialed and/or non-dated alterations have been made to the oath or declaration, and that correction is required.

Applicant submits herewith a Supplemental Oath and Declaration, thus, obviating the Examiner's objection.

35 U.S.C. § 112, 1st Paragraph

Claims 1-34, 47-50 and 57-60

The Examiner has rejected claims 1-34, 47-50 and 57-60 under 35 U.S.C. § 112, first paragraph for lack of enablement. Specifically, the Examiner contends that the claims are missing method steps critical or essential to the practice of the invention and that the specification does not enable one of skill in the art to practice the claimed invention without undue experimentation.

First, applicants have canceled claim 29, thus obviating the rejection with respect to this claim.

Second, applicants have amended claims 1 (and therefore dependent claims 2-28, 30-34 and 57-60) to recite a method for repairing a defect locus in a nonarticular cartilage tissue comprising the step of administering an osteogenic device comprising an osteogenic protein of SEQ ID NO: 6 in a biocompatible, bioresorbable carrier to the defect locus, thereby inducing the formation of functional replacement cartilage tissue to repair said defect, with the proviso that the osteogenic protein of SEQ ID NO: 6 may not be GDF-5 or GDF-6. GDF-5 is also known as CDMP-1 or BMP-14. GDF-6 is also known as CDMP-2 or BMP-13.

Similarly, applicants have amended claim 47 (and therefore dependent claims 48-50 and 57-60) to recite a method of promoting chondrogenesis at a nonarticular defect locus comprising the step of administering an osteogenic device comprising an osteogenic protein of SEQ ID NO: 6 in a devitalized cartilage carrier into the defect locus, thereby inducing the formation of functional cartilage tissue, with the proviso that the osteogenic protein of SEQ ID NO: 6 may not be GDF-5 or GDF-6. Support for these amendments is provided at page 14, line 16 to page 17, line 10 of the specification.

Applicants respectfully submit that the specification provides adequate enablement for the amended claims. For example, the specification at pages 20-21 describes various formulations and methods of administration. The specification at these pages describes that the osteogenic device may be administered by injection or by surgical means such as implantation (*see*, e.g., page 20, lines 27-30). Thus, one of skill in the art would be able to practice the claimed invention without any undue experimentation.

Accordingly, applicants respectfully request that the Examiner withdraw this enablement rejection.

35 U.S.C. § 102(b)

Claims 1-4, 7-11, 14-16, 25, 27, 47, 48, 57, 59 and 60

The Examiner has rejected claims 1-4, 7-11, 14-16, 25, 27, 47, 48, 57, 59 and 60 under 35 U.S.C. § 102(b) as being anticipated by WO 96/14335 ("Luyten"). The Examiner states that Luyten discloses that CDMP-1 and CDMP-2 have *in vivo* chondrogenic activity in combination with a matrix for the repair of cartilage. The Examiner further states that Luyten teaches that the CDMPs can be combined with a number of suitable carriers and that the formulation can be administered via an injection.

Applicants have amended claims 1 and 47 (and therefore dependent claims 2-28, 30-34, 48-50 and 57-60) to recite the osteogenic protein of SEQ ID NO: 6 wherein said recited proteins do not include GDF-5 (CDMP-1) and GDF-6 (CDMP-2). Accordingly, applicants respectfully request that the Examiner withdraw this novelty rejection.

35 U.S.C. § 103(a)

Claims 1-6, 7-25, 27, 30-34, 47, 48, 57 and 59-60

The Examiner has rejected claims 1-6, 7-25, 27, 30-34, 47, 48, 57 and 59-60 under 35 U.S.C. § 103(a) as being obvious over Luyten in view of WO 95/16035 ("Celeste") and Cui

et al., "Repair of thyroid cartilage defect with bone morphogenetic protein," Annals of Otology, Rhinology and Laryngology, 106, pp. 326-328 (1997) ("Cui"). The Examiner states that Luyten discloses CDMP-1 and CDMP-2 having *in vivo* chondrogenic activity in combination with a matrix for the repair of cartilage. The Examiner also states that Luyten teaches that CDMPs can be combined with a number of suitable carriers such as fibrin glue, cartilage grafts and collagen and that the formulation can be administered via an injection. The Examiner states that Celeste teaches pharmaceutically acceptable carriers such as collagen, PLA, polymers of lactic acid, PGA and carboxymethylcellulose and that BMPs are useful in treating tendon or ligament defects as well as the formation of bone, cartilage, and tendon. The Examiner further states that Cui teaches the repair of thyroid cartilage defect with BMP by administering BMP for the replacement of lost laryngotracheal cartilage which results in new bone formation. The Examiner, therefore, concludes that it would have been obvious to one skilled in the art to arrive at the claimed invention by combining the teachings of the cited references because all the references teach BMPs for inducing replacement growth of defects in cartilaginous tissues.

As described above, applicants have amended claim 1 and 47 (and claims dependent therefrom) to recite a method for repairing a defect locus in a nonarticular cartilage tissue and a method for promoting chondrogenesis at a nonarticular defect locus, respectively, comprising the step of administering an osteogenic device comprising an osteogenic protein of SEQ ID NO: 6 in a biocompatible, bioresorbable carrier, with the proviso that the osteogenic protein of SEQ ID NO: 6 may not be GDF-5 or GDF-6.

Luyten discloses the use of CDMP-1 and CDMP-2 for stimulating chondrogenic activity without substantially stimulating osteogenic activity. Luyten does not teach or suggest the use of any other osteogenic proteins for repairing nonarticular cartilage tissue or for promoting chondrogenesis at a nonarticular defect locus, as recited in the amended claims. Neither Celeste nor Cui remedies this deficiency. Celeste discloses that BMP-12 (GDF-7) and BMP-13 (GDF-6) either alone or in combination with other BMPs induce tendon/ligament-like tissue healing and repair. Celeste does not teach or suggest that BMP-12 or BMP-13 may be used to repair nonarticular cartilage or promote chondrogenesis at a nonarticular defect locus. Cui teaches that bovine BMP

repairs a thyroid cartilage defect by inducing new bone formation which fills the defect in the cartilage. Nothing in Cui teaches or suggests that the bovine BMP induces or promotes functional replacement cartilage tissue.

Thus, nothing in Luyten, Celeste or Cui, either alone or in combination, teaches a method for repairing a defect locus in a nonarticular cartilage tissue or a method of promoting chondrogenesis at a nonarticular defect locus as recited in any of the amended claims. Moreover, there is nothing in any of Luyten, Celeste or Cui to motivate the skilled worker to combine the teachings of these publications. And, even if there were a motivation to combine these publications, the skilled worker would not have arrived at the claimed invention. Accordingly, applicants request that the Examiner withdraw this obviousness rejection.

CONCLUSION

In view of the foregoing remarks and amendments, applicants request that the Examiner favorably reconsider this application and allow the claims pending herein. If the Examiner believes that a telephone conference would expedite allowance of this application, she is invited to telephone the undersigned at any time.

Respectfully submitted,

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